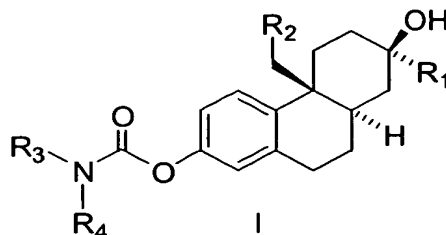


CLAIMS

1. A compound of Formula I



a prodrug of said compound, or a pharmaceutically acceptable salt of said compound or prodrug;

wherein R₁ is a) -(C₁-C₆)alkyl optionally substituted with -CF₃, b) -C≡C-CH₃, c) -C≡C-Cl, d) -C≡C-CF₃, e) -CH₂O(C₁-C₄)alkyl optionally substituted with -CF₃ or f) -CF₃;

R₂ is a) -(C₁-C₅)alkyl, b) -(C₂-C₅)alkenyl or c) -phenyl optionally substituted with one of the following: -OH, -NR₉-C(O)-(C₂-C₄)alkyl, -CN, -Z-het, -O-(C₁-C₃)alkyl-C(O)-NR₉R₁₀, -NR₉-Z-C(O)-NR₉R₁₀, -Z-NR₉-SO₂-R₁₀, -NR₉-SO₂-het, -O-C(O)-(C₁-C₄)alkyl or -O-SO₂-(C₁-C₄)alkyl;

Z for each occurrence is independently -(C₀-C₄)alkyl;

R₃ is a) -hydrogen, b) -(C₁-C₆)alkyl optionally substituted with one to three halo, c) -(C₂-C₆)alkenyl or d) -(C₂-C₆)alkynyl optionally substituted with one to three halo;

R₄ is a) -hydrogen, b) -(C₂-C₅)alkyl-NR₅R₆ or c) -(C₀-C₅)alkyl-het;

or R₃ and R₄ are taken together with N to form het;

R₅ and R₆ are each independently a) hydrogen or b) -(C₁-C₃)alkyl;

het is an optionally substituted 5-, 6- or 7-membered saturated, partially saturated or unsaturated heterocyclic ring containing from 1 to 3 heteroatoms selected from the group consisting of nitrogen, oxygen and sulfur; and including any bicyclic group in which any of the above heterocyclic rings is fused to a benzene ring or another heterocyclic ring; and optionally substituted with one to four R₇; provided that het is other than pyridinyl, imidazolyl or tetrazolyl;

R₇ is a) -(C₁-C₆)alkyl optionally substituted with one to three R₈, b) -Z-NR₉R₁₀ or c) -Z-C(O)-NR₉R₁₀;

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R₈ for each occurrence is independently a) halo, b) -OH, c) oxo or d) -O(C₁-C₆)alkyl;

R₉ and R₁₀ for each occurrence are independently a) -H or b) -(C₁-C₃)alkyl; or R₉ and R₁₀ are taken together with N to form het;

5 provided that:

1) when R₁ is -C≡C-CH₃, R₂ is phenyl and R₃ is hydrogen, then R₄ is other than -(CH₂)₂-N(CH₃)₂, -(CH₂)₃-N(CH₃)₂, -(CH₂)₂-pyrrolidinyl optionally substituted with methyl, -(CH₂)₃-pyrrolidinyl or -(CH₂)₂-morpholinyl;

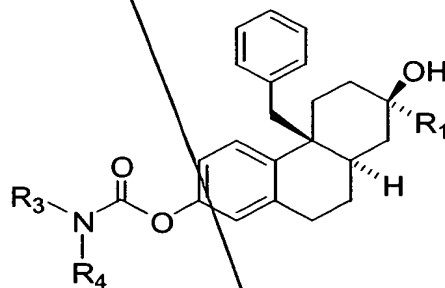
2) when R₁ is -C≡C-CH₃, R₂ is -CH₂-CH=CH₂ and R₃ is hydrogen, then R₄ is other than -(CH₂)₂-pyrrolidinyl;

3) when R₁ is -C≡C-CH₃, R₂ is propyl and R₃ is hydrogen, then R₄ is other than -(CH₂)₂-N(CH₃)₂ or -(CH₂)₂-pyrrolidinyl;

4) when R₁ is -C≡C-CH₃, R₂ is butyl and R₃ is hydrogen, then R₄ is other than -(CH₂)₂-N(CH₃)₂, -(CH₂)₂-pyrrolidinyl or -(CH₂)₂-morpholinyl; and

5) when R₁ is -C≡C-CH₃, R₂ is pentyl and R₃ is hydrogen, then R₄ is other than -(CH₂)₂-morpholinyl or -(CH₂)₂-pyrrolidinyl.

2. A compound of claim 1 of Formula II



II

20 a prodrug of said compound or a pharmaceutically acceptable salt of said compound or prodrug;

wherein R₁ is a) -(C₁-C₆)alkyl optionally substituted with -CF₃, b) -C≡C-CH₃, c) -CF₃ or d) -CH₂O(C₂-C₄)alkyl.

3. A compound of claim 2 wherein R₁ is a) -CH₂CH₂CH₃, b) -C≡C-CH₃ or c) -CF₃.

4. A compound of claim 3

wherein R₃ is a) hydrogen, b) methyl, c) ethyl, d) propyl or e) isopropyl;

R₄ is -(C₂-C₃)alkyl-NR₅R₆;

R₅ and R₆ are each independently a) methyl, b) ethyl, c) propyl or d) isopropyl.

5. A compound of claim 4

wherein R₃ is a) methyl, b) ethyl, c) propyl or d) isopropyl;

5 R₄ is -(C₂-C₃)alkyl-NR₅R₆;

R₅ and R₆ are each independently a) methyl, b) ethyl, c) propyl or d) isopropyl.

6. A compound of claim 5

wherein R₃ is a) methyl or b) ethyl;

10 R₄ is -(C₂-C₃)alkyl-NR₅R₆;

R₅ and R₆ are each methyl.

7. A compound of claim 3

wherein R₃ is a) hydrogen, b) methyl or c) ethyl;

R₄ is -(C₀-C₄)alkyl-het;

15 het is a) morpholinyl, b) pyrrolidinyl, c) piperidinyl, d) piperazinyl, e)

hexahydro-azepinyl, f) azabicyclo[2.2.2]oct-3-yl, g) azabicyclo[3.2.1]oct-3-yl, h) 3,6-diazabicyclo[3.1.1]heptyl or i) 2,5-diazabicyclo[2.2.1]heptyl;

the above het groups are optionally substituted with one to four R₇;

R₇ is a) methyl, b) ethyl or c) -NR₉R₁₀;

20 R₉ and R₁₀ are each independently methyl or ethyl.

8. A compound of claim 7

wherein R₃ is a) hydrogen, b) methyl or c) ethyl;

R₄ is -(C₀-C₃)alkyl-het;

25 het is a) morpholinyl, b) pyrrolidinyl, c) piperidinyl, d) hexahydro-azepinyl, or e) azabicyclo[3.2.1]oct-3-yl;

the above het groups are optionally substituted with one or two R₇;

wherein R₇ is a) methyl or b) ethyl.

9. A compound of claim 8

wherein R₃ is a) methyl or b) ethyl;

30 R₄ is -(C₀-C₃)alkyl-het;

het is a) pyrrolidinyl, b) piperidinyl, c) hexahydro-azepinyl, or d) azabicyclo[3.2.1]oct-3-yl;

the above het groups are optionally substituted with one R₇;

wherein R₇ is a) methyl or b) ethyl.

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10. A compound of claim 3 wherein R_3 and R_4 are taken together with N to form het;

wherein het is a) piperazinyl, b) pyrrolidinyl, c) piperidinyl, d) 2,5-diazabicyclo[2.2.1]heptyl, e) azetidiny, f) 1,4-diazabicyclo[3.2.2]nonanyl, g) 3,6-diazabicyclo[3.2.2]nonanyl, h) octahydro-pyrido[1,2-a]pyrazinyl or i) hexahydro-1,4-diazepinyl;

the above het groups are optionally substituted with one or two R_7 ;

R_7 is a) $-(C_1-C_2)$ alkyl optionally substituted with one or two R_8 , b) $-(C_0-C_2)$ alkyl- NR_9R_{10} or c) $-Z-C(O)-NR_9R_{10}$;

10 R_8 is -OH;

R_9 and R_{10} are each independently a) hydrogen b) methyl or c) ethyl;

or R_9 and R_{10} are taken together with N to form a) pyrrolidinyl or b) piperidinyl.

11. A compound of claim 10 wherein R_3 and R_4 are taken together with N to form het;

15 wherein het is a) pyrrolidinyl, b) piperidinyl or c) azetidinyl;

the above het groups are optionally substituted with one R_7 ;

R_7 is $-CH_2-NR_9R_{10}$;

R_9 and R_{10} are each independently a) methyl or b) ethyl;

or R_9 and R_{10} are taken together with N to form a) pyrrolidinyl or b)

20 piperidinyl.

12. A compound of claim 1

wherein R_1 is a) $-CH_2CH_2CH_3$, b) $-C\equiv C-CH_3$ or c) $-CF_3$;

R_2 is a) $-(C_1-C_5)$ alkyl or b) $-(C_2-C_5)$ alkenyl;

R_3 is a) hydrogen, b) methyl, c) ethyl, d) propyl or e) isopropyl;

25 R_4 is $-(C_2-C_3)$ alkyl- NR_5R_6 ;

R_5 and R_6 are each independently a) methyl, b) ethyl, c) propyl or d) isopropyl.

13. A compound of claim 12

wherein R_2 is a) methyl, b) ethyl, c) propyl, d) ethenyl, e) propenyl or f) butenyl;

30 R_3 is a) hydrogen, b) methyl or c) ethyl,

R_5 and R_6 are each independently a) methyl or b) ethyl.

14. A compound of claim 1

wherein R_1 is a) $-CH_2CH_2CH_3$, b) $-C\equiv C-CH_3$ or c) $-CF_3$;

R_2 is a) $-(C_1-C_5)$ alkyl or b) $-(C_2-C_5)$ alkenyl;

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R₃ is a) hydrogen, b) methyl, c) ethyl, d) propyl or e) isopropyl;
R₄ is -(C₀-C₄)alkyl-het;
het is a) morpholinyl, b) pyrrolidinyl, c) piperidinyl or d) piperazinyl;
the above het groups are optionally substituted with one or two R₇;
5 R₇ is a) methyl, b) ethyl or c) -NR₉R₁₀;
R₉ and R₁₀ are each independently methyl or ethyl.

15. A compound of claim 14
wherein R₂ is a) methyl, b) ethyl, c) propyl, d) ethenyl, e) propenyl or f) butenyl;
R₃ is a) hydrogen, b) methyl or c) ethyl;
10 R₄ is -(C₂-C₃)alkyl-het;
het is a) morpholinyl or b) pyrrolidinyl;
the above het groups are optionally substituted with one or two R₇;
wherein R₇ is a) methyl or b) ethyl.

16. A compound of claim 1

15 wherein R₁ is a) -CH₂CH₂CH₃, b) -C≡C-CH₃ or c) -CF₃;
R₂ is a) -(C₁-C₅)alkyl or b) -(C₂-C₅)alkenyl;
R₃ and R₄ are taken together with N to form het;
het is a) piperazinyl, b) pyrrolidinyl or c) piperidinyl;
the above het groups are optionally substituted with one or two R₇;
20 R₇ is a) -(C₁-C₂)alkyl optionally substituted with one or two R₈, b) -(C₀-
C₂)alkyl-NR₉R₁₀ or c) -Z-C(O)-NR₉R₁₀;
R₈ is -OH;
R₉ and R₁₀ are each independently a) hydrogen b) methyl or c) ethyl;
or R₉ and R₁₀ are taken together with N to form a) pyrrolidinyl or b)
25 piperidinyl.

17. A compound of claim 16
wherein R₂ is a) methyl, b) ethyl, c) propyl, d) ethenyl, e) propenyl or f) butenyl;
het is a) pyrrolidinyl or b) piperidinyl;
the above het groups are optionally substituted with one R₇;
30 R₇ is -CH₂-NR₉R₁₀;
R₉ and R₁₀ are each independently a) methyl or b) ethyl;
or R₉ and R₁₀ are taken together with N to form a) pyrrolidinyl or b)
piperidinyl.

18. A compound of claim 1 wherein in Formula I -CH₂-R₂ is ethenyl or ethynyl.

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19. A compound of claim 4 selected from the group consisting of:
carbamic acid, [2-(dimethylamino)ethyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [3-(dimethylamino)propyl]-, (4bS,7R,8aR)-
5 4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester; and

carbamic acid, [3-(diethylamino)propyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester.

20. A compound of claim 6 selected from the group consisting of:

10 carbamic acid, [2-(dimethylamino)ethyl]methyl-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [2-(dimethylamino)ethyl]methyl-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-

15 phenanthrenyl ester;

carbamic acid, [3-(dimethylamino)propyl]ethyl-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester; and

carbamic acid, [2-(dimethylamino)ethyl]ethyl-, (4bS,7R,8aR)-
20 4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester.

21. A compound of claim 8 selected from the group consisting of:

carbamic acid, [2-(1-pyrrolidinyl)ethyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

25 carbamic acid, [2-(1-piperidinyl)ethyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [3-(hexahydro-1H-azepin-1-yl)propyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

30 carbamic acid, [3-(1-pyrrolidinyl)propyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [2-(1-pyrrolidinyl)ethyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

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carbamic acid, [2-(1-piperidinyl)ethyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

carbamic acid, (1-ethyl-3-piperidinyl)-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl;

5 carbamic acid, [(3-*exo*)-8-methyl-8-azabicyclo[3.2.1]oct-3-yl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [(1-ethyl-2-pyrrolidinyl)methyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

10 carbamic acid, [3-(hexahydro-1*H*-azepin-1-yl)propyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

carbamic acid, [[[2*R*]-1-ethyl-2-pyrrolidinyl]methyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [3-(1-piperidinyl)propyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

carbamic acid, [3-(1-pyrrolidinyl)propyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

carbamic acid, [[[2*S*]-1-ethyl-2-pyrrolidinyl]methyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

carbamic acid, [[[2*R*]-1-ethyl-2-pyrrolidinyl]methyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-propyl-2-phenanthrenyl ester;

carbamic acid, [2-(4-morpholinyl)ethyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester; and

30 carbamic acid, [3-(4-morpholinyl)propyl]-, (4b*S*,7*R*,8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester.

22. A compound of claim 11 selected from the group consisting of:

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1-pyrrolidinecarboxylic acid, 2-(1-pyrrolidinylmethyl)-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

5 1-piperidinecarboxylic acid, 2-(1-piperidinylmethyl)-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

1-piperidinecarboxylic acid, 2-[(dimethylamino)methyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester;

10 1-piperidinecarboxylic acid, 2-[(diethylamino)methyl]-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester; and

15 1-azetidinecarboxylic acid, 3-(1-piperidinyl)-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester.

23. Carbamic acid, (2,2,6,6-tetramethyl-4-piperidinyl)-, (4bS,7R,8aR)-4b,5,6,7,8,8a,9,10-octahydro-7-hydroxy-4b-(phenylmethyl)-7-(trifluoromethyl)-2-phenanthrenyl ester, a compound of claim 7.

20 24. A compound of claim 13 selected from the group consisting of: carbamic acid, (3-dimethylaminopropyl)methyl-, (4bS, 7R, 8aR)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester;

25 carbamic acid, (2-dimethylaminoethyl)methyl-, (4bS, 7R, 8aR)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester;

carbamic acid, (2-dimethylaminoethyl)ethyl-, (4bS, 7R, 8aR)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester; and

30 carbamic acid, (2-dimethylaminoethyl)-, (4bS, 7R, 8aR)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester.

25. A compound of claim 15 selected from the group consisting of:

carbamic acid, (3-morpholin-4-yl-propyl)-, (4bS, 7R, 8aR)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester;

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carbamic acid, (2-morpholin-4-yl-ethyl)-, (4b*S*, 7*R*, 8a*R*)-4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynyl-phenanthren-2-yl ester.

- 5 26. 2-Pyrrolidin-1-ylmethylpyrrolidine-1-carboxylic acid, (4bS, 7R, 8aR)-
4b,5,6,7,8,8a,9,10-octahydro-4b-ethyl-7-hydroxy-7-prop-1-ynylphenanthren-2-yl
ester, a compound of claim 17.
27. A method for the treatment of a glucocorticoid receptor-mediated disease or
condition in a mammal, which comprises administering to the mammal a
10 therapeutically effective amount of a compound of claim 1, a prodrug thereof, or a
pharmaceutically acceptable salt of said compound or prodrug.
28. The method of claim 27 wherein the glucocorticoid receptor-mediated
disease or condition is selected from the group consisting of obesity, diabetes,
depression, anxiety and neurodegeneration.
- 15 29. The method of claim 28 wherein the condition is obesity.
30. The method of claim 29 which further comprises administering a β_3 agonist,
a thyromimetic agent, an eating behavior modifying agent or a NPY antagonist.
31. The method of claim 30 wherein the eating behavior modifying agent is
orlistat or sibutramine.
- 20 32. The method of claim 28 wherein the disease is diabetes.
33. The method of claim 32 which further comprises administering an aldose
reductase inhibitor, a glycogen phosphorylase inhibitor, a sorbitol dehydrogenase
inhibitor, insulin, a sulfonylurea, glipizide, glyburide, or chlorpropamide.
34. The method of claim 27 wherein the glucocorticoid receptor-mediated
25 disease is an inflammatory disease.
35. A pharmaceutical composition comprising a therapeutically effective amount
of a compound of claim 1, a prodrug of said compound or a pharmaceutically
acceptable salt of said compound or prodrug; and a pharmaceutically acceptable
carrier, vehicle or diluent.
- 30 36. A pharmaceutical combination composition comprising: a therapeutically
effective amount of a composition comprising:
a first compound, said first compound being a compound of claim 1, a
prodrug of said compound or a pharmaceutically acceptable salt of said compound,
or prodrug;

a second compound, said second compound being a β_3 agonist, a thyromimetic agent, an eating behavior modifying agent or a NPY antagonist; and a pharmaceutical carrier, vehicle or diluent.

37. A kit comprising:

5 a) a first compound, said first compound being a compound of claim 1, a prodrug of said compound or a pharmaceutically acceptable salt of said compound, or prodrug and a pharmaceutically acceptable carrier, vehicle or diluent in a first unit dosage form;

10 b) a second compound, said second compound being a β_3 agonist, a thyromimetic agent, an eating behavior modifying agent or a NPY antagonist; and a pharmaceutically acceptable carrier, vehicle or diluent in a second unit dosage form; and

c) a container for containing said first and second dosage forms; wherein the amounts of said first and second compounds result in a therapeutic effect.

15 38. A method for inducing weight loss in a mammal which comprises administering to the mammal a therapeutically effective amount of a compound of claim 1, a prodrug of said compound or a pharmaceutically acceptable salt of said compound or prodrug.

20 39. A pharmaceutical combination composition comprising: a therapeutically effective amount of a composition comprising:

a first compound, said first compound being a compound of claim 1, a prodrug of said compound or a pharmaceutically acceptable salt of said compound or prodrug;

25 a second compound, said second compound being an aldose reductase inhibitor, a glycogen phosphorylase inhibitor, a sorbitol dehydrogenase inhibitor, insulin, a sulfonylurea, glipizide, glyburide, or chlorpropamide; and

a pharmaceutical carrier, vehicle or diluent.

30 40. A method for the treatment of an inflammatory disease in a mammal which comprises administering to said mammal a therapeutically effective amount of a compound of claim 1, a prodrug of said compound or a pharmaceutically acceptable salt of said compound or prodrug.

41. The method of claim 40 wherein the inflammatory disease is selected from the group consisting of arthritis, asthma, rhinitis and immunomodulation.

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